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May 19, 2005

Stephen L. Johnson, Administrator
US Environmental Protection Agency
Ariel Rios Building #1101-A
1200 Pennsylvania Avenue, NW
Washington, DC 20460

Subject: Comments on the HPV test plan for Tetrahydrobenzaldehyde

Dear Administrator Johnson:

The following comments on Dow's test plan for the chemical tetrahydrobenzaldehyde are submitted on behalf of the Physicians Committee for Responsible Medicine, People for the Ethical Treatment of Animals, the Humane Society of the United States, the Doris Day Animal League, and Earth Island Institute. These health, animal protection, and environmental organizations have a combined membership of more than ten million Americans.

The Dow Chemical Company submitted its test plan on Dec. 17, 2004 for tetrahydrobenzaldehyde (CAS No. 100-50-5), also known as THBA. This chemical is produced by reacting butadiene and acrolein with a catalyst. THBA is then used as an intermediate in the production of a single final product. It would be useful to know the identity of the final product and how it is used in commerce; Dow does not mention this in the test plan. Nevertheless, Dow has submitted a comprehensive analysis of THBA by compiling existing data from a variety of sources, and using *in silico* estimation models, to fulfill almost all SIDS endpoints. A separate reproductive/developmental toxicity study was not located but Dow states that these tests are unnecessary due to the corrosive nature of this chemical and very limited exposure for humans. We support this type of hazard and exposure analysis and concur with Dow that no additional testing is required.

Specifically, this material was corrosive to the skin in a DOT study with rabbits. These and other findings have resulted in adequate measures to protect workers from occupational exposure to THBA. This chemical has an odor threshold of approximately 0.22 ppm, which can be detected well in advance of the established exposure limit of 5 ppm. Additional animal studies will not likely change the potential for exposure, which is already minimal. Moreover, oral administration is not a likely route of exposure for humans, and any additional animal testing for reproductive/developmental endpoints would have to proceed via inhalation or via a dermal study. However, based on existing acute toxicity findings, this chemical appears to be irritating to the skin and eyes and corrosive to the skin. Thus, animal testing via OECD 421 is inappropriate via the dermal or inhalation route. This is an important point because chemicals that are classified as

caustic will not likely cause systemic toxicity at doses that do not also cause significant local effects. The interpretation of any systemic effects that may be observed in proposed reproductive or developmental studies will be confounded by local effects due to the irritancy of the compound. Since it has been reported in the developmental toxicology literature that maternal stress may be related to developmental effects, it would be difficult to infer causation in the event of a positive result with THBA. Other public commenters have pointed to this at other times and chemicals with such properties should not be subject to further testing in animals. The EPA has accepted this principle in its consideration of other HPV test plans on similarly corrosive chemicals.

We commend Dow on a thoughtful analysis of the toxicity of THBA to determine whether any new testing will result in useful information. The EPA has also stated that participants "may conclude that there is sufficient data, given the totality of what is known about a chemical, including human experience, that certain endpoints need not be tested" and "as with all chemicals, before generating new information, participants should further consider whether any additional information obtained would be useful or relevant" (Wayland, 1999; *Federal Register* 2000).

We commend the sponsor on a well-written, thorough test plan for THBA and concur that additional animal studies are not warranted. Thank you for your attention to these comments. I may be reached at 202-686-2210, ext. 327, or via e-mail at *meven@pcrm.org*.

Sincerely,

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Research Analyst

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